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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,180	12/09/2005	Richard Joseph Fagan	C&R-108	1199

23557 7590 10/03/2007

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
10/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,180	FAGAN ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-66* is/are pending in the application.

4a) Of the above claim(s) *47-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46,65 and 66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *46-66* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/27/07 & 10/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's election of Group I invention filed on 20 August 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's further election with traverse of SEQ ID NO:10 filed on 20 August 2007 is acknowledged. The traversal is on the ground(s) that both SEQ ID NO:10 and 12 should be examined in the subject application as SEQ ID NO:12 is a portion of subsequence of SEQ ID NO:10. This argument is persuasive, and the restriction requirement between SEQ ID NO:10 and 12 is withdrawn.

Currently, claims 46-66 are pending, and claims 46, 65 and 66 will be examined to the extent that they read on the elected invention. Claims 47-64 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

Information Disclosure Statement

Applicant's IDSs submitted on 8/27/07 and 10/2/06 are acknowledged and have been considered. A signed copy is attached hereto.

Priority acknowledgement

This application is a national stage entry (371) of PCT/GB03/05621 with the international filing date of 12/19/03, which is acknowledged.

Specification

The specification is objected to for the following informalities, appropriate correction is required for each item:

On page 7, lines 20-21, it states "the invention provides a *ligand* which binds specifically to protein members of the IL-8 like chemokine family of the first aspect of the invention". Since a chemokine itself is considered a "ligand", it is unclear what "a *ligand* which binds specifically to protein members of the IL-8 like chemokine" is meant.

Claims

Claim 46 is objected to for encompassing a non-elected subject matter: parts b)-h) and j)-o); and SEQ ID NO:2, 4, 6 and 8 in parts 7)-13) of part a). The applicant is required to amend the claims to read only upon the elected invention.

Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 46, 65 and 66 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 46, 65 and 66 are directed to a composition comprising an isolated polypeptide or a polypeptide of SEQ ID NO:10 or 12, and a variant (% or functional equivalent) or fragment thereof. The polypeptide is assumed a member of IL-8-like cytokine family.

The specification discloses two INSP094 splicing variants, SEQ ID NO:8 and 10, and a C-terminal fragment thereof, SEQ ID NO:12. Based on its sequence homology to the known human IL-18, the specification indicates that said polypeptides are IL-8 like chemokines (page 5, lines 17-23, and page 3, lines 4-5, for example), and thus the polypeptides *may be* useful, for example, in the treatment or prevention of numerous diseases/disorders, such as those recited on page 6 of the specification. However, the specification does not disclose any information about the functional property or biological significance directly associated with any of the INSP094 polypeptides, nor the receptor for the so-called IL-8 like chemokine.

Thus, the asserted therapeutic or preventative uses for the claimed polypeptides based on sequence homology to a known molecule are not considered substantial as generally the art acknowledges that the function of a protein cannot be predicted based solely on structural similarity to a known protein. For example, in the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) discloses that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β

family members BMP-2 and TGF- 1 had no effect on metanephrogenesis under identical conditions (page 9023, paragraph bridging columns 1-2). As another example, IL-18 receptor (IL-18R) was thought to be another IL-1 receptor (IL-1R) base on the sequence homology, and therefore, designated IL-1 receptor-related protein (IL-1Rrp) when it was first discovered, and its ligand was unknown (Parnet et al., J. Biol. Chem., 1996, 271(8): 3967-70). The IL-1Rrp is now known as IL-18 receptor, has distinct ligand, and possesses distinct functional properties from that of IL-1R even though it is a member of IL-1R family. Further, the claims recite "functions as a member of the IL-8-like chemokine family" (parts 2) and 5) of part a), for example), and specification defines such "polypeptides that comprise amino acid sequence or structural features that can be identified as conserved features within the polypeptides of the IL-8 like chemokine family, such that the polypeptide's interaction with ligand is not substantially affected detrimentally in comparison to the function of the full length wild type polypeptide". It seems that the term is defined based on structural features of the molecules. The prior art search reveals that IL-8, based on structural features, belong to CXC chemokine family, which has many members with diverse functional properties. Therefore, the structural similarity does not necessarily indicate functional similarity, and in the instant case, the established utility for IL-8 cannot be automatically applied to said IL-8 like chemokine in the absence of any supporting evidence.

Clearly, further research and experimentation is required to identify or confirm the therapeutic uses of the INSP094 polypeptides of SEQ ID NO:10 and 12, such as its association to specific diseases or conditions, which can then be so diagnosed or treated using said polypeptides. There is no immediately apparent or "real world" utility for the INSP094 polypeptides of SEQ ID NO:10 and 12. However, it is a matter of law that the claimed invention must be useful in its currently available form. According to MPEP, a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not considered a substantial utility.

The instant situation is analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. ... a patent is not a hunting license. ... [i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a polypeptide of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support the assertion that the INSP094 polypeptides of SEQ ID NO:10 and 12 were, as of the filing date, useful for the treatment of any disease/disorder, as stated at page 6 of the specification, for example. Therefore, there was no "real world" use for the claimed polypeptides as of the filing date. Upon further research, a specific, and substantial utility might be found for the claimed isolated polypeptides. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

> The following is a quotation of the first paragraph of 35 U.S.C. 112:
>
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46, 65 and 66 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Further, *even if* the specification taught how to use the claimed polypeptides, enablement would not be commensurate in scope with claim 46, which encompass functional equivalents (parts 3), 6), 7) and 10)-12) of part a), for example), and % variants/fragments of SEQ ID NO:10 or 12 (parts 8)-13) of part a), for example), wherein the functional equivalents are not required to have any structural similarity to the recited polypeptide sequences (parts 3) and 6), for example), and % variants/fragments of SEQ ID NO:10 or 12 are not required to have any functional activity (parts 8) and 9), for example). The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claim.

Claim 46 (part a)) encompasses functional equivalents and % variants/fragments of SEQ ID NO:10 or 12, which read on any or all molecules including those without any sequence similarity to the recited sequence (for functional equivalents), such as structurally unrelated polypeptides or small molecules; and any variant/fragment meeting the sequence limitation, and with or without any functional activity (for % variants/fragments). The claim encompasses an unreasonable number of distinct molecules, and inoperative polypeptides. However, the specification provides no guidance or working examples as to how the skilled artisan could make the encompassed functional equivalents, or use an inactive variant/fragment of SEQ ID NO:10 or 12, as no functional limitation is associated with the variants in the claim.

Due to the large quantity of experimentation necessary to generate the infinite number of functional equivalents recited in the claim and possibly screen the same for activity (*if* the specification had disclosed a functional property for the INSP094 polypeptides), and to determine how to use the inoperative polypeptides, the lack of direction/ guidance presented in the specification regarding same, the absence of working examples directed to same, the complex and unpredictable nature of the invention, and the breadth of the claims which embrace a broad class of structurally unrelated molecules, and structurally diverse variants without functional limitation, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope, *even if* the specification had taught how to use the INSP094 polypeptides of SEQ ID NO:10 and 12.

Claim 46 is further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Part a) of the claim encompasses functional equivalents (parts 3), 6), 7) and 10)-12), for example) and % variants/fragments (parts 8)-12), for example) of SEQ ID NO:10 or 12, which read on any or all molecules including those without any sequence similarity to the recited sequence (for functional equivalents), such as structurally unrelated polypeptides or small

molecules; and any variant/fragment meeting the sequence limitation, and with or without any functional activity (for % variants/fragments). Further, the recited limitation "functions as a member of the IL-8-like chemokine family" is not meaningful because it is unclear what "IL-8-like chemokine family" encompasses, and there is no specific functional property for the INSP094 polypeptides of SEQ ID NO:10 and 12 has ever been disclosed. Thus, the claim encompasses a genus of molecules with unrelated structures and unknown functional activity (a functional equivalent), and a genus of polypeptides that are defined only by partial amino acid sequence identity (% variants/fragments).

The specification discloses two INSP094 splicing variants, SEQ ID NO:8 and 10, and a C-terminal fragment thereof, SEQ ID NO:12. No other INSP094 variant meeting the limitations of the claim was ever identified or particularly described.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, with respect to functional equivalents, none of the factors is present in the claim as the functional property of the polypeptides is unknown. With respect to % variants/ fragments, the only factor present in the claim is a partial nucleic acid structure in the form of a recitation of percent identity, and there is not even structural identification of the polypeptide from which variants are derived, or identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, with the exception of SEQ ID NO:10 and 12, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides and

the recited "functional equivalent", and therefore conception is not achieved, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides having amino acid sequence set forth in SEQ ID NO:10 or 12, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. This is particularly important in absence of a specific known activity. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131

USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 46 part a) recites the broad recitation that a fragment or a functional equivalent "has greater than 80% (90%) sequence identity with an amino acid sequence" (parts 8) - 11), for example), and the claim also recites a polypeptide comprising "an amino acid sequence comprising that recited in SEQ ID NO:10 or 12" (part 1), for example), and "a fragment of SEQ ID NO:10 or 12" (part 2), for example), which are the narrower statements of the range/limitation. Additionally, part 12) of part a) recites "the functional equivalent of 3), 6), 7), 10), or 11), wherein the functional equivalent exhibits *significant structural homology* with a polypeptide". According to the definition in the specification, the term "significant structural homology" means that two proteins to share structural homology with a certainty of 10% and above (page 14). However, parts 10) and 11) already recite much narrower (than 10%) range or limitation as to sequence homology, 80% and 90%, respectively. Separate claims are suggested.

The claim is further indefinite for the recitation that a fragment "functions as a member of the IL-8-like chemokine family" (parts 2) and 5) of part a), for example) because it is unclear what it is meant, and what function is indicated. A definition of such is noted in the specification, which refer to "polypeptides that comprise amino acid sequence or structural features that can be identified as conserved features within the polypeptides of the IL-8 like chemokine family, such that the polypeptide's interaction with ligand is not substantially affected detrimentally in comparison to the function of the full length wild type polypeptide". However, such a definition does not clearly define any functional activity. Given the fact that it is not well established as to what defines "IL-8 like chemokine family", and there are many members with diverse functional properties in the CXC chemokine family (to which IL-8 belongs), the metes and bounds of the claim, therefore, cannot be determined. The claim is further indefinite for the recitations "a functional equivalent of" (parts 3) and 6) of part a), for example), and "an active fragment" (parts 8)-11) of part a), for example) because neither the specification nor the claim defines a functional activity of the polypeptide, therefore, it is unclear what "a functional equivalent" or "an active fragment" thereof would encompass, thus, metes and bounds of the claim cannot be determined.

Further, the term "homologous" in part 7) (for example) of part a) of the claim is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear up to what percentage of sequence identity it is still considered "homologous to".

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 46 is rejected under 35 U.S.C. 102(e) as being anticipated by Ratcliffe et al. (US7,238,860, provided in the last Office Action mailed on 7/20/07).

Ratcliffe discloses a polypeptide, SEQ ID NO:342, which comprises amino acids 12-19 of the present SEQ ID NO:10 with 100% sequence identity (see computer printout of the search results). Additionally, Ratcliffe teaches fragments of the polypeptide, which is at least 5 to about 15 amino acids (column 7, lines 10-14). Therefore, the reference anticipates the claim (part 2) of part a), for example).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang, Ph.D.
Patent Examiner
AU1646
9/28/07